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TESTS OF PREDNISONE

Can the physician safely prescribe prednisone by generic name rather than by trade name? To help answer this much-debated question, The Medical Letter purchased samples of 5-mg. prednisone tablets from 29 different pharmaceutical companies and had them tested for conformance to U.S. Pharmacopeia (XV) standards by a competent commercial laboratory. The samples represented all of the "name" brands, and about half of other listed suppliers selected at random.

THE TESTS - The Pharmacopeia permits a variation of plus or minus 10 per cent from the labeled quantity of prednisone in the tablets; of 20 tablets in each sample, no tablet may vary from the average weight by more than 20 per cent, and not more than two tablets may vary from the average by more than 10 per cent. The Pharmacopeia also provides a 30-minute time limit for the *in vitro* disintegration of the tablets under specified conditions.

All of the "name"-brand samples were within the USP tolerances, as were most of the others. Four of the 29 samples were substandard (see table on next page); two of these showed excessive variation in the amount of prednisone present in the tablets, one containing 86 per cent of declared weight, the other 132 per cent. Because of inherent limitations in the accuracy of the USP test, the lower amount must be considered a borderline case, but the higher amount is clearly excessive. The other two substandard samples did not meet the requirements for disintegration. Additional samples were purchased from the four companies whose tablets were substandard and subjected to the same tests. Three of the four new samples met all of the requirements of the standard; the remaining sample contained slightly less prednisone than the permissible minimum.

EFFECT OF DEVIATIONS - As for the clinical significance of the deviations, the excessive amount of prednisone in the first of the two samples obtained from Cowley Pharmaceuticals might, in some instances, present a problem. The below-standard weights of one of the original 29 samples and of the second Cowley sample were borderline and of no clinical significance. While the disintegration test is a severe one, the failure of the first samples obtained from West-ward and Bryant to disintegrate under the test conditions might in some instances be reflected in reduced absorption of the drug. In general, however, the risk involved in prescribing prednisone by generic name appears to be small. Particularly where the high cost of the "name" brands offers a serious burden to the pa-

RESULTS OF TESTS OF 5-MG. PREDNISONE TABLETS

Note: All samples except those marked with an asterisk conformed fully to the requirements of USP XV; all samples met the requirements for uniformity of weight of tablets. USP XV sets no limits on the amount of cortisone or other foreign steroids in prednisone tablets (see page 65). The prices given are those paid by the pharmacist who purchased the samples for The Medical Letter.

Company	Prednisone found		Cortisone found	Price paid per 100
	Mg.	% of 5 mg.		
Allen Pharmacal	5.07	101.4	less than 1%	2.45
American Drug Products	5.46	109.2	approx. 9%	7.10
American Pharmaceutical	4.53	90.6	less than 1%	3.33
Approved Pharmaceutical	4.63	92.6	less than 1%	2.79
Arlington-Funk (U.S. Vitamin)	5.14	102.8	less than 1%	5.50
Bell Pharmacal	4.89	97.8	approx. 2%	6.00
Bio Intrasol	4.53	90.6	approx. 7%	1.70
Bryant Pharmaceutical: *1st sample(1)	5.14	102.8	approx. 8%	2.40
Bryant Pharmaceutical: 2nd sample (2)	4.72	94.4	(not tested)	2.05
Columbia Medical	4.74	94.8	approx. 8%	2.85
Cowley Pharmaceuticals: *1st sample(3)	6.60	132.0	approx. 7%	5.69
Cowley Pharmaceuticals: *2nd sample(4)	4.42	88.3	(not tested)	5.65
Robert Daniels: *1st sample(4)	4.31	86.2	approx. 7%	2.40
Robert Daniels: 2nd sample(5)	4.82	96.3	(not tested)	2.05
DuMont Pharmacal	4.58	91.6	approx. 1%	4.18
Gotham Pharmaceutical	4.80	96.0	less than 1%	4.40
Italian Drugs Importing	4.55	91.1	less than 1%	10.05
Kirkman Pharmacal	5.22	104.4	approx. 7%	4.75
Lustgarten	5.01	100.2	approx. 9%	3.69
Merck (Deltra)	5.12	102.4	less than 1%	17.90
H. L. Moore	4.74	94.8	approx. 9%	3.08
Parke, Davis	4.97	99.4	less than 1%	17.90
Penhurst Pharmacal	5.46	109.2	approx. 1%	7.28
Philadelphia Ampoule	5.21	104.2	approx. 6%	1.99
Premo Pharmaceutical	4.99	99.8	approx. 2%	3.00
Schering (Meticorten)	4.71	94.2	less than 1%	17.90
Upjohn (Deltasone)	5.00	100.0	less than 1%	17.90
Vitamin Research	4.80	96.0	approx. 7%	3.41
Vitarine	5.34	106.8	approx. 1.5%	3.80
Wales	4.62	92.4	less than 1%	2.58
West-ward: *1st sample(1)	4.99	99.8	less than 1%	4.34
West-ward: 2nd sample(2)	4.85	97.1	(not tested)	2.83
Wolins Pharmacal	4.53	90.6	approx. 7%	2.10

(1) Did not meet requirements for disintegration.
(2) Disintegration satisfactory.
(3) Prednisone content in excess of tolerance.
(4) Prednisone content below tolerance (borderline).
(5) Prednisone content satisfactory.

tient, generic-name prescribing would appear to be in order. While drug stores are unable to pass on to the patient all of the saving with the lower-priced brands, it can nevertheless amount to many dollars on each hundred tablets.

FOREIGN STEROIDS - The sixteenth revision of the U.S. Pharmacopeia, which becomes effective on October 1st, will add a new requirement for prednisone tablets. During storage there is some breakdown of prednisone to cortisone, and the new standard will stipulate that not more than 2 per cent of cortisone or other foreign steroids may be present. Although the requirement is not yet official, and does not apply to the samples covered in this report, tests for foreign steroids were performed on all of the original 29 samples.

Twelve samples (see table) showed amounts of cortisone above 2 per cent, but in no case was the amount sufficient to have any clinical significance. With the highest amount of cortisone found in any of the samples tested, a patient on 40 mg. of prednisone daily (two to four times the usual maintenance dose) would get less than 4 mg. of cortisone per day. Since the maintenance dose of cortisone is usually about 50 to 100 mg. per day, it is unlikely that 4 mg. could have a significant salt-and-water-retaining effect. Nevertheless, physicians have the right to expect that the drugs they prescribe will conform to official standards, and new tests of prednisone will be made in the coming months.

(This is the first in a series of test reports on prescription drugs. Tests of secobarbital are now being made. Medical Letter readers are invited to suggest other drugs they would like to have included in the test program.)

DORMISON, PLACIDYL AND VALMID

Among the non-barbiturate sedative-hypnotic drugs introduced in recent years, three are central-nervous-system depressants belonging to the family of "tertiary carbinols." These are methylparafynol (Dormison - Schering), ethchlorvynol (Placidyl - Abbott), and ethinamate (Valmid - Lilly). All are claimed to offer important advantages over the barbiturates.

DORMISON - This drug was originally recommended for hypnotic use in dosages of 250 mg. Doses of 500 to 1000 mg. were later recommended. An early study (P. R. A. May and F. G. Ebaugh, Am. J. Psychiatry, 109:881, 1953) found the drug safe and "highly efficient" as a hypnotic, but the dosages used were as high as 2.5 grams. In a later review of experience with the drug, one of the same authors (F. G. Ebaugh, Postgrad. Med., 19:513, 1956) concluded that it was both potentially hazardous and ineffective as a hypnotic, a conclusion with which Medical Letter consultants agree.

PLACIDYL - A bedtime dose of 500 mg. of Placidyl is claimed to bring sleep in from 15 minutes to an hour, with hypnotic effect lasting for five hours, and with a low incidence of hangover and other side effects. In one study, the drug was found to be effective as a hypnotic in about 75 per cent of 151 patients treated with various doses, but the study was uncontrolled (C. R. Rein and R. Fleischmajer, AMA Arch. Dermatol., 75:438, 1957). Side effects, which caused

nine per cent of the patients to discontinue further dosage, included hangover, ataxia, vertigo, headache, nausea, and vomiting. L. Lasagna (The Effects of Pharmacologic Agents on the Nervous System, Chapt. 19, Williams & Wilkins, 1959) finds that Placidyl "can provide adequate performance [as a hypnotic] but...must usually be given in 1.0 Gm. doses..."

VALMID - This drug, it is claimed, induces sleep within 15 to 30 minutes, with a four-hour span of action. The manufacturer recommends a hypnotic dose of one or two 500-mg. tablets. One favorable study (E. L. Foltz, et al., Am. J. Med. Sci., 230:528, 1955) showed occasional side effects such as "mental obtundity," fatigue, sweating, headache, nausea and heartburn, abdominal cramps, pain, dizziness, nervousness and anxiety. Lasagna (see above) equated Valmid with Placidyl as providing adequate hypnosis, but usually requiring one-gram doses.

While Dormison appears to be ineffective, Placidyl and Valmid appear to be acceptable alternatives to a short-acting barbiturate for both sedation and hypnosis. Adequately controlled studies which would permit a reliable judgment as to the relative frequency and severity of side effects with these drugs and the barbiturates are lacking. Since patients differ in their reactions to different drugs, however, if a patient suffers excessive hangover or other side effects from a barbiturate, one of these drugs (or Noludar - see The Medical Letter, 2:35, 1960) might well be tried. In quantities of 30, a 500-mg. capsule of Placidyl or a 500-mg. tablet of Valmid costs about 9¢ (or 18¢ for a 1000-mg. dose), and a 100-mg. capsule of secobarbital costs about 4¢ to 8¢.

FURTHER NOTE ON ALTAFUR

In a preliminary appraisal of the antibacterial drug furaltadone (Altafur - Eaton) nearly a year ago, The Medical Letter (1:75, Oct. 2, 1959) warned that experience with the drug was very limited, and that it belonged to a group which had "sufficient potential for serious toxicity...to make the use of Altafur in office practice inadvisable at this time." A reappraisal of the drug in the last issue (2:62, 1960) pointed out that "Altafur is being more widely used than is warranted by available clinical data," and called for further evidence as to its effectiveness and safety. The question of safety has now been definitively answered in a circular letter received from the manufacturer while the last issue was on the press.

As the result of side reactions reported to the manufacturer, the circular letter says, "We have drastically revised our labeling for the preparation...the use of Altafur should be confined to infections that are not amenable to other drugs now available to you." In view of the hazard, and of the questionable effectiveness of the drug, Medical Letter consultants advise against any use of Altafur.

From the beginning, Altafur has been promoted as a drug with a "low order of side effects," and it has recently been advertised as "a 'first choice' antimicrobial" (JAMA, July 30, 1960). The history of Altafur emphasizes the need for special caution by physicians in the use of all new drugs, and for a high degree of skepticism toward claims for safety which have not been confirmed by wide and prolonged use.

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